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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/053,530	LEDBETTER ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-44,48,102-106 and 142-148* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-44,48,102-106 and 142-148* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. In a telephonic conversation with Applicants' representative, Greta E. Noland on 04 April 2007, it was brought to the examiner's attention that the previous Office action mailed 23 March 2007 did not consider the amendment filed 21 March 2007. Accordingly, the Office Action mailed 23 March 2007 is hereby VACATED and the period for reply begins from the mailing of this Office Action. Ex parte Gourtoff, 1924 C.D. 153, 329 O.G. 536 (Comm'r Pat. 1924).

2. Claims 1-22, 45-47, 49-101 and 107-141 are cancelled.

Claims 23-24, 35-36 and 38 have been amended.

Claims 146--148 have been added.

3. Claims 23-44, 48, 102-106 and 142-148 are pending and under consideration.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. This Office Action contains New Grounds of Rejections.

Withdrawn Objections/Rejections

6. The objection to the specification in the use of trademarks is withdrawn in view of the amendments to the specification filed 12/12/2006.

7. The objection to the specification as misspelling the term "protei" is withdrawn in view of the amendment to the specification filed 12/12/2006.

8. The objection to claims 35-36 and 38 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn in view of the amendments to the claims.

9. The rejection of claims 39-44, 47-48 and 142 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation "wherein said binding domain polypeptide is a single chain Fv capable of binding CD20" in claim 39 is withdrawn in view of the amendments to the claims.

10. The rejection of claims 23, 25-44, 47-48, 102-106 and 142-145 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation "wherein said hinge

peptide is an IgG or IgA hinge peptide in which the number of cysteine residues is reduced to two, provided that when the hinge peptide contains two cysteines the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally occurring IgG or IgA antibody is not deleted or substituted..." is withdrawn in view of the amendments to the claims.

11. The rejection of claims 23-26, 31-33 and 143-145 under 35 U.S.C. 102(e) as being anticipated by Gillies et al (U. S. Patent Application Publication US 2003/0044423A1, with priority to 60/274,096, 3/7/01, cited on PTO-892 mailed 8/27/04) is withdrawn in view of applicants' arguments and the amendments to the claims which require preservation of the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain.

12. The rejection of claims 23, 25-28, 31-34, 39, 142 and 143-145 under 35 U.S.C. 102(a) as being anticipated by Wu et al (Protein Engineering 14(12):1025-1033, 2001, IDS filed 6/7/04) is withdrawn in view of applicants' arguments and amendments to the claims.

13. The rejection of claims 27-28, 34, 40-41, 44, 47 and 102-103 under 35 U.S.C. 103(a) as being unpatentable over Gillies et al (U. S. Patent Application Publication US 2003/0044423A1, with priority to 60/274,096, 3/7/01, cited on PTO-892 mailed 8/27/04) in view of Shan et al (The Journal of immunology, 162:6589-6595, 1999, IDS reference EA filed 7/12/02) and Liu et al (The Journal of Immunology, 139(10):3521-3526, 1987, IDS filed 6/7/04) is withdrawn in view of the amendments to the claims which require preservation of the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain.

14. The rejection of claims 30, 35-36 and 38 under 35 U.S.C. 103(a) as being unpatentable over Gillies et al (U. S. Patent Application Publication US 2003/0044423A1, with priority to 60/274,096, 3/7/01, cited on PTO-892 mailed 8/27/04) in view of Kucherlapati et al (US Patent 6,150,584, filed 10/2/96) and Gilliand et al (Tissue Antigens, 47:1-20, 1996, IDS filed 6/7/04) is withdrawn in view of the amendments to the claims which require preservation of the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain.

15. The rejection of claims 48 and 104-106 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gillies et al (U. S. Patent Application Publication US 2003/0044423A1, with priority to 60/274,096, 3/7/01, cited on PTO-892 mailed 8/27/04) in view of Fell et al (The Journal of Biological Chemistry, 267(22):15552-15558, 1992) and Gilliand et al (Tissue Antigens, 47:1-20, 1996, IDS filed 6/7/04) is withdrawn in view of the amendments to the claims which require preservation of the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain.

Priority

The following is reiterated for convenience. The disclosure of a single specific species in prior application USSN 60/367,358 does not provide adequate written support for the myriad of other species of single chain proteins of the present claims, including those that bind to CD19, CD22, CD30 ligand, CD54, CD106, CD2, CD5, CD10, CD27, CD28, CD40, CTLA-4, 4-1BB, 4-1BB ligand, IFN-gamma, IL-4, Il-12, IL-17, IL-17 receptor, CD59, CD48, CD72, CD70, CD86/B7.2, CD40 ligand, CD43, CD83, DEC-205, VLA-4, HER1, HER2, HER3, HER4, EGFR, VEGF, VEGFR, IGF-I, IGF-II, transferrin receptor, estrogen receptor, progesterone receptor, follicle stimulating hormone receptor, rectinoic acid receptor, MUC-1, NY-ESO-1, NA 17-A, Melan-A/MART-1, tyrosinase, Gp-100, MAGE, BAGE, GAGE, CTA class receptors, the HOM-MEL-40 antigen encoded by the SSX2 gene, CEA and PyLT. Further, the present claims are drawn to any IgG or an IgA hinge peptide where the priority application uses an IgG1 hinge and there is no disclosure in the priority document wherein the hinge peptide is an IgG or IgA in which the number of cysteine residues is reduced to one *and wherein the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally occurring IgG or IgA antibody is not deleted or substituted.* Thus, not even the presently claimed CD20 single chain proteins are adequately disclosed in a manner consistent with the first paragraph of 35 U.S.C 112. Again, prior application USSN 60/367,358 discloses the anti-CD20 2H7 scFv fused to human IgG1 hinge-CH2-CH3 as well as 2H7 scFv fused with CD154, which

does not provide adequate written support the broader claims of the present application as discussed supra. Therefore, the effective filing date of the presently claimed subject matter is deemed to be that of the instant application, i.e., 1/17/2002. If applicant desires priority prior to 1/17/2002; applicant is invited to point out and provide documentary support for the priority of the instant claims. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

New Grounds of Objections/Rejections

15. Claims 23-44, 48, 102-106 and 142-148 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

As currently presented base claims 23 and 24 recite that the single chain protien comprises a binding domain polypeptide comprisng an IgG hinge peptide in which the number of cysteine residues is two and the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally occurring IgG antibody is not deleted or substituted. The exclusionary proviso wherein the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally occurring IgG antibody is not deleted or substituted appears to have been added in the amendment filed 10/28/2003. The response filed 6/7/2004 states that support can be found throughout the specification, specifically at pp. 10-11, 16, 25, 29, 38, ect, ect and Figs 4, 11,1 3, 19 and 20. This has been fully considered but is not found persuaisve. The pages and figures as pointed to by applicant generically disclose mutated hinge regions containing one or two cysteine residues and the disclsoure of a scFv- IgG1, in which the hinge cysteines were mutatetd to serine residues by site-directed mutagenesis and the construct in which the human IgG1 hinge region was substituted with a portion of the human IgA hinge (e.g., Ex. 5,

Fig. 11) and the assessment of ADCC and CDC does not provide adequate written support for the currently claimed limitations, i.e., wherein the first cysteine of the IgG hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally occurring IgG antibody is not deleted or substituted because there is insufficient guidance and direction to the subgenus of single chain proteins comprising such. Further, at pg. 29, lines 16-19 of the as filed specifiation it states "The Cys residue of the hinge which makes a disulfide bond with a corresponding Cys of the light chain, to hold the heavy and light chains of the native antibody molecule, can be deleted or, preferably is substituted with, e.g., a Pro residue or the like." The as filed specification, drawings and claims do not disclose a single species of a single chain polypeptide comprising a binding domain polypeptide comprisng an IgG hinge peptide in which the number of cysteine residues is two and the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally occurring IgG or IgA antibody is not deleted or substituted and the disclsoed preference for its substitution does not provide adequate writtten support for the currently cliemd limitations. Further, Tan et al (Proc. Natl. Acad. Sci. USA, 87:162-166, January 1990) indicate that human IgG3 and IgG4 have the disulfide bridge between heavy and light chains crossing from the carboxyl end of the light chain to a cysteine in the homologous position in either the IgG3 or IgG4 CH1 domain (see pg. 165, top of 2nd col.). Clearly applicant was not in possession of the full subgenus of IgG hinge peptides in which the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally occurring IgG antibody is not deleted or substituted. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

The claims now recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the presently amended claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written

support for the limitations recited in the present claims in the specification or claims, as filed, or remove these limitations from the claims in response to this Office Action.

16. Claims 23-44, 48, 102-106 and 142-148 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using the immunoglobulin fusion proteins that mediate ADCC and CDC with the Fc comprising an IgG1 or IgG3 hinge and IgG1 CH2-CH3 domains, does not reasonably provide enablement for the genus of binding domain polypeptides comprising an IgG hinge and just any CH2 and CH3 domains having the property of mediating ADCC. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are drawn to a single chain protein comprising a binding domain polypeptide comprising an immunoglobulin CH2 constant region polypeptide, a CH3 constant region polypeptide and an IgG hinge wherein the first hinge cysteine responsible for forming a disulfide bond with the light chain constant region is not substituted or deleted, and wherein the fusion protein binds a variety of different target antigens and promotes antibody dependent cell-mediated cytotoxicity or complement fixation or both. Thus, the claims encompass single chain proteins for promoting or mediating antibody dependent cell-mediated cytotoxicity or complement fixation or both,

wherein the single chain protein comprises an IgG hinge and just any CH2 and CH3 regions.

The specification teaches making a 2H7 scFv fused to human IgG1 hinge, CH2 and CH3 regions, wherein the single-chain protein mediates antibody dependent cell-mediated cytotoxicity and complement fixation (see Examples). The specification does not teach the genus of single-chain proteins comprising any targeting polypeptide including single-chain antibodies that bind various cell surface antigens (e.g., claims 28-30, 35-38, 146-149) and comprising an IgG hinge wherein the first hinge cysteine responsible for forming a disulfide bond with the light chain constant region is not substituted or deleted, and comprising just any CH2 and CH3 domains wherein the single chain protein promotes antibody dependent cell-mediated cytotoxicity or complement fixation or both. There are no working examples of a single-chain protein comprising any targeting polypeptide including single-chain antibodies that bind various cell surface antigens (e.g., claims 28-30, 35-38, 146-149) and comprising an IgG hinge wherein the first hinge cysteine responsible for forming a disulfide bond with the light chain constant region is not substituted or deleted, and just any CH2 and CH3 regions wherein the single chain protein promotes antibody dependent cell-mediated cytotoxicity or complement fixation or both. The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970).

The state of the prior art is such that the effector functions of a given IgG are intricately linked to the presence and properties of its hinge region. Surprisingly, despite having been the object of study for over 20 years, the precise relationship between these parameters and complement activation is still unclear Dall'Acqua et al, pg. 1129, 1st col., The Journal of Immunology, 177:1129-1138, 2006. Gillies et al (US Patent 7,148,321 B2, cited on PTO-892 mailed 3/23/2007), disclose:

> "IgM and IgA do not mediate ADCC. To construct a polyvalent antibody or Ig fusion that mediates ADCC" (col. 16, lines 51-53].

Tan et al (Proc. Natl. Acad. Sci. USA, 87:162-166, January 1990), disclose that IgG4 with the IgG3 hinge is as flexible as wild-type IgG3 but is unable to activate complement (pg. 165 2nd col.).

Thus, in view of the art recognized lack of ADCC activity associated with the IgA Fc region and a lack of complement activation for all IgG, one of ordinary skill in the art could not predictably extrapolate the teachings in the specification limited to a 2H7 scFv-huIgG1 Fc region that mediates ADCC and CDC to the genus of single-chain proteins comprising an IgG hinge and just any CH2 and CH3 domains, inclusive to domains that do not mediate ADCC and/or complement.

Therefore, in view of the broadly claimed invention, the lack of predictability in the art as evidenced by Gillies, and lack of guidance in the specification with regard to using the fusion proteins comprising IgA-CH2-CH3 domains for mediating ADCC, one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention.

Response to Arguments

The Declaration of Dr. Alan F Wahl under 37 CFR 1.132 filed 31 March 2007 is insufficient to overcome the rejection because the showing is not commensurate in scope with the claimed invention. The skilled artisan could not extrapolate the findings in the declaration limited to an IgG1 or IgG3 hinge region, combined with IgG1 CH2 and CH3 regions to the genus of IgG hinges and just any CH2 and CH3 regions, particularly in view of the evidence of Gillies that IgM and IgA do not mediate ADCC and Tan et al that IgG4 with the IgG3 hinge is unable to activate complement. Further, the evidence in the Declaration does not establish a nexus between not deleting or substituting the first cysteine of the hinge region that is responsible for forming a disulfide bond with the light chain constant region with the biological properties (i.e., ADCC and CDC) and the genus of IgG hinges, and just any CH2 and CH3 domains, particularly where the first cysteine of the hinge region does not form a disulfide with the light chain constant region as in human IgG3 and IgG4 (Tan et al, Proc. Natl. Acad. Sci., USA, 87:162-166, January 1990).

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 23-44, 48, 102-106 and 142-148 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-53 of copending Application No.11/088,693. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The instant claims are drawn to a single-chain protein comprising a binding domain polypeptide capable of binding to a target biological molecule, said binding domain polypeptide being joined to a hinge peptide, said hinge peptide being joined to an immunoglobulin heavy chain CH2 constant region polypeptide, said CH2 constant region polypeptide being joined to an immunoglobulin heavy chain CH3 constant region polypeptide, wherein said hinge peptide is an IgG or IgA hinge peptide wherein the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally-occurring IgG or IgA antibody is not deleted or substituted or wherein the IgG or IgA hinge peptide contains one cysteine, and wherein said single

chain protein (1) is capable of binding to said target, and (2) is capable of promoting antibody dependent cell-mediated cytotoxicity or complement fixation or both and wherein the binding domain polypeptide is a single-chain antibody that binds to a variety of different cell surface antigens.

Claims 1-53 of copending Application No.11/088,693 are drawn to a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a single-chain protein comprising a binding domain polypeptide capable of binding to a target biological molecule, said binding domain polypeptide being joined to a hinge peptide, said hinge peptide being joined to an immunoglobulin heavy chain CH2 constant region polypeptide, said CH2 constant region polypeptide being joined to an immunoglobulin heavy chain CH3 constant region polypeptide, wherein said hinge peptide is an IgG or IgA hinge peptide wherein the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally-occurring IgG or IgA antibody is not deleted or substituted or wherein the IgG or IgA hinge peptide contains one cysteine, and wherein said single chain protein (1) is capable of binding to said target, and (2) is capable of promoting antibody dependent cell-mediated cytotoxicity or complement fixation or both and wherein the binding domain polypeptide is a single-chain antibody that binds to a variety of different cell surface antigens. Applicant is reminded that "comprising" s inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See MPEP 2111.03. Thus, claims 1-53 of copending Application No.11/088,693 are drawn to a species that reads upon the claims in the instant application and are drawn to an invention that is not patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

19. Claims 24-44, 48, 102-106 and 142-148 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22 of copending Application No.10/207,655 in view of Shan et al (The Journal of immunology, 162:6589-6595, 1999, IDS reference EA filed 7/12/02) and Liu et al (The

Journal of Immunology, 139(10):3521-3526, 1987, IDS filed 6/7/04). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The instant claims have been described supra.

Claims 1-22 of copending Application No.10/207,655 are drawn to a binding domain-immunoglobulin fusion protein, comprising a binding domain polypeptide fused to a mutated human IgG1 hinge region comprising one cysteine residue, said hinge region being joined to an immunoglobulin heavy chain CH2 constant region polypeptide, said CH2 constant region polypeptide being joined to an immunoglobulin heavy chain CH3 constant region polypeptide, and wherein said binding domain-immunoglobulin fusion protein specifically binds to an antigen and promotes antibody dependent cell-mediated cytotoxicity or complement fixation or both, wherein the binding domain polypeptide comprises a light chain variable region and a heavy chain variable region and binds various different cell surface antigens. Claims 1-22 copending Application No.10/207,655 do not specifically teach wherein the binding domain polypeptide is a 2H7 scFv. This deficiency is made up for in the teachings of Shan et al and Liu et al.

Shan et al teach an anti-CD20 scFv-IgG1 wherein the VH and VL domains are joined by a 15 amino acid linker. Shan et al also teach CD20 antibodies do not internalize after cell surface binding, anti-CD20 antibodies are not shed from the cell surface and CD20 is expressed at a high density on more than 95% of all B cell lymphomas and the antigenic density of CD20 is relatively homogenous from one tumor to another (see Shan et al, pg. 6594, top left column)

Liu et al teach the VH and Vk sequences of monoclonal antibody 2H7 that specifically targets CD20 expressed on B cell lymphomas.

The claims in the instant application are obvious variants of claims 1-22 copending Application No.10/207,655 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to produce a binding domain-immunoglobulin fusion protein, comprising a 2H7 scFv fused to a mutated human IgG1 hinge region comprising one cysteine residue, said hinge region being joined to an immunoglobulin heavy chain CH2 constant region polypeptide, said CH2 constant region polypeptide being joined to an immunoglobulin heavy chain CH3

constant region polypeptide, wherein said the 2H7 scFv-IgG promotes antibody dependent cell-mediated cytotoxicity or complement fixation or both for therapeutic benefit in lymphoma patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to produce a binding domain-immunoglobulin fusion protein, comprising a 2H7 scFv fused to a mutated human IgG1 hinge region comprising one cysteine residue, said hinge region being joined to an immunoglobulin heavy chain CH2 constant region polypeptide, said CH2 constant region polypeptide being joined to an immunoglobulin heavy chain CH3 constant region polypeptide, wherein said the 2H7 scFv-IgG promotes antibody dependent cell-mediated cytotoxicity or complement fixation or both for therapeutic benefit in lymphoma patients in view of claims 1-22 copending Application No.10/207,655 and Shan et al and Liu et al because Shan et al teach an anti-CD20 scFv-IgG1 wherein the VH and VL domains are joined by a 15 amino acid linker Liu et al teach the VH and Vk sequences of monoclonal antibody 2H7 that specifically targets CD20 expressed on B cell lymphomas and according to Shan CD20 antibodies do not internalize after cell surface binding, anti-CD20 antibodies are not shed from the cell surface and CD20 is expressed at a high density on more than 95% of all B cell lymphomas and the antigenic density of CD20 is relatively homogenous from one tumor to another. Therefore, one of ordinary skill in the art would have been motivated at the time the invention was made to modify the binding domain-immunoglobulin fusion proteins of claims 1-22 copending Application No.10/207,655 to produce a 2H7 scFv-IgG promotes antibody dependent cell-mediated cytotoxicity or complement fixation or both for therapeutic benefit in lymphoma patients since CD20 antibodies do not internalize after cell surface binding, anti-CD20 antibodies are not shed from the cell surface and CD20 is expressed at a high density on more than 95% of all B cell lymphomas and the antigenic density of CD20 is relatively homogenous from one tumor to another. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced a binding domain-immunoglobulin fusion protein, comprising a 2H7 scFv fused to a mutated human IgG1 hinge region comprising one cysteine residue, said hinge region

being joined to an immunoglobulin heavy chain CH2 constant region polypeptide, said CH2 constant region polypeptide being joined to an immunoglobulin heavy chain CH3 constant region polypeptide, wherein said the 2H7 scFv-IgG promotes antibody dependent cell-mediated cytotoxicity or complement fixation or both for therapeutic benefit in lymphoma patients in view of claims 1-22 copending Application No.10/207,655 and Shan et al and Liu et al.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 24-44, 48, 102-106 and 142-148 are directed to an invention not patentably distinct from claims 1-22 of commonly assigned copending Application No.10/207,655. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned copending Application No.10/207,655, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

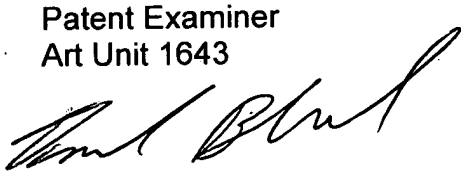
20. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J. Blanchard
Patent Examiner
Art Unit 1643



DB
April 4, 2007